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PATENT
2024738-7030210000
(CYM-034)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:

David Zahniser

Serial No.: 09/430,198

Filed: October 29, 1999

For: APPARATUS AND METHODS FOR
VERIFYING THE LOCATION OF
AREAS OF INTEREST WITHIN A
SAMPLE IN AN IMAGING SYSTEM

)
) **Group Art Unit: 2623**

)
) **Confirmation No.: 6914**

)
) **Examiner: Chong R. Kim**

APPEAL BRIEF-CFR 1.192

ATTN: Board of Patent Appeals and Interferences
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This Brief is in furtherance of the Notice of Appeal filed herewith, and contains the following items in the order indicated below, as required by C.F.R. §1.192:

- I. Real Party in Interest
- II. Related Appeals and Interferences
- III. Status of Claims
- IV. Status of Amendments
- V. Summary of Invention
- VI. Issues
- VII. Grouping of Claims
- VIII. Arguments
- IX. Appendix of Claims Involved in the Appeal

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I. Real Party in Interest

The real party in interest in this appeal is Cytac Corporation, a corporation organized under the laws in the State of Delaware.

II. Related Appeals and Interferences

There are no appeals or interferences that will directly affect, or be directly affected by, or have a bearing on the Board's decision in this appeal.

III. Status of Claims

This application includes claims 1-25. Of these, claims 1-14, 21, and 23-25 are pending, and the remaining claims 15-20 and 22 have been cancelled. All pending claims stand rejected, leaving no claims allowed. The claims on appeal are claims 1-14, 21, and 23-25.

IV. Status of Amendments

All amendments have been entered.

V. Summary of Invention

The inventions, as defined in the claims on appeal, are directed to methods and systems for verifying a location of an area of interest within a sample, such as a cytological specimen deposited on a slide. A datum mark on the sample is located, the area of interest within the sample is identified (e.g., by optically scanning the sample), and the datum mark is relocated. The area of interest location is verified if a dimensional error or spatial offset value in locating the datum mark relative to relocating the datum mark is less than a tolerance value (e.g., ten microns to one thousand microns). If the area of interest location is not verified, the sample may be rejected. Although it should not be limited to the preferred embodiments described in the

specification, the inventions will now be described in terms of a preferred embodiment in order to aid in further understanding the invention.

As illustrated in Fig. 1, a microscope slide 10 has a specimen area 12 on which a cytological specimen 14 is deposited, and at least two fiducial datum marks 16. As illustrated in Fig. 2, one preferred apparatus 30 comprises (1) an image processing system 32 for acquiring images of the specimen 14 and processing those images to identify areas in the specimen 14 most likely to contain certain features of interest, such as cell abnormalities; (2) a review station 36 for allowing a human operator to review the areas of interest identified by the image processing system 32; and (3) a computer server 34 for coordinating information flow between the image processing system 32 to the review station 36.

As illustrated in Fig. 3, the image processing system 32 comprises a (1) first optical system 38, which includes a camera 48 and a microscope 50 for optically imaging the specimen 14; (2) a stage 40 for moving the slide 10 relative to the optical path 51 of the microscope 50, so that the entire specimen 14 can be optically scanned; (3) a robotic slide handler 64 for transferring the slide 10 from a slide cassette to the movable stage 40 for imaging, and then back to the slide cassette; (4) an interface controller 60 for precisely moving the movable stage 40; and (5) an internal computer system 46 for processing the image of the specimen 14, identifying areas of interest within specimen 14, and storing the identified area of interest locations.

To ensure that these area of interest locations can be later identified after the slide 10 is physically transferred to the review station 36, the computer system 46, in a standard manner, registers the datum marks 16 located on the slide 10 within the coordinate system of the image processing system 32. That is, the first datum mark 16 is centered within the field of view of the microscope 50 and assigned a first reference coordinate value, such as (0, 0), and the second

datum mark 16 is centered within the field of view of the microscope 50, and assigned a second reference coordinate value. The entire specimen 14 is then optically scanned to identify the most relevant areas of interest, and coordinate values within the coordinate system established by the datum marks 16 are assigned to the areas of interest, so that these coordinate values can subsequently be referenced in the review station 36. That is, the datum marks 16 will be registered within the coordinate system of the review station 36 in the same manner as the datum marks 16 were registered within the coordinate system of the image processing system 32, and the identified areas of interest will be located in accordance with their coordinate values.

Significant to the invention, the computer system 46 ensures that the area of interest locations are accurate when they are identified to prevent false readings of the specimen 14 at the review station 36, which may otherwise be caused by incorrect handling or positioning of the slides during the image scanning process. The computer system 46 accomplishes by using the data marks 16 in a novel manner.

In particular, after the image scanning process is performed, the computer system 46 determines a spatial offset of the data marks 16 by moving the stage 40 to a location corresponding to the measured reference coordinate value of the first datum mark 16, and thereafter to a second location corresponding to the measured reference coordinate value of the second datum mark 16. Because of a margin of error inherent in any mechanical system, the fiducial marks 16 are typically displaced by some minor spatial offset value. If the spatial offset value is greater than a predetermined tolerance value, either the slide 10 moved relative to the stage 40 during scanning, the system lost position, or some other error occurred, which brings into question the validity of the stored locations of the identified areas of interest. In this case,

the slide 10 is rejected as being the result of an unreliable scan. Otherwise, the area of interest locations are verified.

VI. Issues

A. Whether claims 1-3, 5, and 7-8 are unpatentable under 35 U.S.C. §103 as being obvious over U.S. Patent No. 5,000,554 (“Gibbs”)

B. Whether claims 4, 6, and 9 are unpatentable under 35 U.S.C. §103 as being obvious over Gibbs in view of U.S. Patent No. 5,587,833 (“Kamentsky”)

C. Whether claims 10-14, 20-21, and 23-25 are unpatentable under 35 U.S.C. §103 as being obvious over Gibbs in view of U.S. Patent No. 5,499,097 (“Ortyn”)

VII. Grouping of Claims

Appellant believes that the following groups of claims are patentably distinct from each other:

A. Claims 1-9

B. Claims 10-14, 20-21, and 24

C. Claims 23 and 25

VIII. Arguments

A. Gibbs

Appellant respectfully submits that the Examiner erred in rejecting claims 1-3, 5, and 7-8 under 35 U.S.C. §103 as being obvious over U.S. Patent No. 5,000,554 (“Gibbs”).

Gibbs only describes the prior art method of measuring a datum mark only once to allow an automated optical microscope to repeatedly locate areas of interest on a slide. In particular,

Gibbs discloses a microscope slide 10 having a reference mark 72 that can be used to establish a reference position of the slide 10 relative to a frame 14 on which the slide 10 is mounted within a carrier 12 (col. 5, lines 54-63).

Prior to a slide scanning operation, the reference mark 72 is located approximately within the center of the microscope's field of view via user operation of directional keys 94, 96, 98, and 100, and the positions of moving carriages 20 and 28 within the frame 14 set via operation of a key 116 (col. 9, lines 8-29). A sample 82 carried by the slide 10 can then be automatically scanned, and upon detection of an object of interest within sample 82, the object of interest is placed in the center of the field of view of the microscope via user operation of directional keys 94, 96, 98, and 100, and its x-y coordinates recorded (col. 9, lines 30-46). In this manner, the location of the object of interest relative to the reference mark 72 is known even after the slide 10 has been removed from the carrier 12.

On a later occasion when it is desired to relocate object of interest, the slide 10 is placed back into the carrier 12, the reference mark 72 is located in the center of the field of view of the microscope via user operation of the directional keys 94, 96, 98, and 100, the positions of the carriages 20 and 28 within the frame 14 set via operation of the key 116, and the previously recorded x-y coordinates of the object of interest entered to relocate the object of interest within the center of the microscope's field of view (col. 9, lines 60 to col. 10, line 14). Significantly, Gibbs relocates the object of interest within the center of the field of view of the microscope under the assumption that the originally recorded location of the object of interest is correct.

Thus, it can be appreciated that not only does Gibbs fail to disclose that the accuracy of the object of interest location be verified based on a dimensional error between a location and

relocation of a datum mark, it fails to disclose any means for verifying the accuracy of the location of the object of interest.

In spite of this failed teaching, the Examiner states that Gibbs does disclose a method of verifying the location of the object of interest, and then concludes that it would have been obvious to modify Gibbs to perform the claimed method to perform this verification. In particular, the Examiner states that “Gibbs further discloses that the location of the area of interest is verified when the area of interest is detected ‘at approximately the same location as when it was originally detected.’” (page 5 of Final Office Action, dated October 19, 2004). However, Gibbs does not disclose that the area of interest is verified when the area of interest is detected. Instead, Gibbs discloses that the “detected microscopic object appears in the microscope’s visual field at approximately the same location as when it was originally detected.” (col. 10, lines 3-6). This is not a verification of the accuracy of the location of the detected microscopic object. It is merely a statement that the machine is designed, such that the microscopic object is supposed to appear in the visual field of the microscope. If the location of the detected microscopic object is indeed inaccurate, the machine will wrongly assume that it will appear in the visual field of the microscope, because there is no verification of that location.

In the recent Advisory Action, the Examiner, in support of the conclusion that Gibbs does verify the location of the area of interest, defines the term “verify” as “to determine or test the truth or accuracy.” This definition only serves to support Appellant’s contention that Gibbs does not verify the location of the area of interest, since the Gibbs device nowhere determines or tests the truth or accuracy of this location of the area of interest. The Examiner goes on to state in the Advisory Action that Gibbs discloses that there could be a dimensional error, and that “the dimensional error will determine the accuracy of the location of the area of interest”; “that is, that

the accuracy of the location of the area of interest is based on a dimensional error in locating the datum relative to relocating the datum,” and thus, “Gibbs appears to disclose a verification of the location of the area of interest.” However, Gibbs just states the problem. That is, a dimensional error between locating and relocating the datum will cause the accuracy of the location of the area of interest to suffer. Appellant fails to see how the Examiner can construe this problem statement to mean that the location of the area of interest is actually verified.

In addition, even if Gibbs could somehow be construed to verify the location of the area of interest after the datum is relocated, it is the relocation of the area of interest that would be verified—not the original location of the area of interest. That is, claim 1 requires that the area of interest location that is verified be the area of interest location that is determined relative to the mark. The area of interest that is relocated in Gibbs (that is, the area of interest that is verified under the Examiner’s interpretation of Gibbs), is not determined at all. Rather, the Gibbs device is merely designed to place the area of interest, whose location is input into the system, and is thus already known, within the field of view of the microscope.

Having concluded that the Gibbs device verifies the location of the area of interest based on a dimensional error between the location and relocation of the datum mark, the Examiner then concludes that it would have been obvious to verify the location of the area of interest if the dimensional error is less than a tolerance value. In making this conclusion, the Examiner, in the Advisory Action, states that “Gibbs also discloses that the verification (accuracy) of the location of the area of interest is based on the dimensional error.” It is unclear why the Examiner equates the term “accuracy” with the term “verification,” since they clearly mean two different things. However, as previously stated above, the Gibbs device not only fails to verify the location of the area of interest based on a dimensional error between the location and relocation of the datum

mark, it fails to verify the location of an area of interest at all. That is, merely recognizing that the accuracy of a location of an area of interest is affected by a dimensional error is clearly not the same as verifying the area of interest location.

Given the foregoing, Appellant submits that independent claim 1, as well as the claims depending therefrom (claims 2-3, 5, and 7-8), are patentable over Gibbs.

B. Gibbs and Kamentsky

Appellant respectfully submits that the Examiner erred in rejecting claims 4, 6, and 9 under 35 U.S.C. §103 as being obvious over Gibbs in view of U.S. Patent No. 5,587,833 (“Kamentsky”). In particular, Kamentsky does not supplement the lack of teaching in Gibbs that the verification of the location of an area of interest be based on the dimensional error between datum mark measurements. Given this, Appellant submits that claims 4, 6, and 9 are patentable over the combination of Gibbs and Kamentsky.

C. Gibbs and Ortyn

Appellant respectfully submits that the Examiner erred in rejecting claims 10-14, 20-21, and 23-25 under 35 U.S.C. §103 as being obvious over Gibbs in view of U.S. Patent No. 5,499,097 (“Ortyn”). In particular, as stated above, Gibbs neither discloses nor suggests the verification of an area of interest, as required by independent claims 10, 14, 20, and 24. To the extent that the Examiner relies on Ortyn for the verification teaching or the datum location and relocation teaching, Appellant incorporates the arguments presented in the Amendment and Response, dated April 9, 2004, and the Amendment after Final, dated December 17, 2004. Given this, Appellant submits that independent claims 10, 14, 20, and 24, as well as the claims

depending therefrom (claims 11-13, 21, 23, and 24), are patentable over the combination of Gibbs and Ortyn.

In addition, claim 23 and 25 respectively require the methods of claims 14 and 24 to be performed while the slide is continuously mounted within the imaging system. Although the Examiner stated that Ortyn discloses a method that is performed while the slide is continuously mounted within the imaging system (see page 12 of Final Office Action), this is not the method that the Examiner relies on in rejecting claims 14 and 24. That is, the Examiner relies on the method disclosed in Gibbs, which is performed during two different optical scans. That is, the slide is mounted in a microscope, where the datum mark and object of interest are located, and then the slide is removed and mounted within another microscope (or the same microscope), where the datum mark and object of interest are relocated. If it is the Examiner's contention that the method performed by the Gibbs device be completely replaced with the method disclosed in Ortyn, there is no such suggestion, since Ortyn teaches locating and relocating a datum mark on a calibration slide—not a slide with a biological specimen. In addition, such a modification would completely eviscerate the object of the Gibbs device, which is to provide an improved method for identifying objects of interest and then subsequently reviewing those objects of interest. In sum, there is absolutely no suggestion in Ortyn to locate an area of interest and locate and relocate a datum mark while the slide is continuously mounted within the imaging system.


Thus, the additional patentable features recited in claims 23 and 25 provide a further basis for the patentability of these claims over the combination of Gibbs and Ortyn.

Respectfully submitted,

Bingham McCutchen LLP

Dated: 4/5/05

By:


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IX. Appendix of Claims Involved in the Appeal

1. A method for verifying a location of an area of interest within a sample, the method comprising:

locating a datum mark on the sample;

identifying the area of interest within the sample;

determining the location of the area of interest relative to the mark; and

relocating the datum, wherein the location of the area of interest is verified if a dimensional error in locating the datum relative to relocating the datum is less than a tolerance value.

2. The method according to claim 1 wherein the identification of the area of interest within the sample comprises optically scanning the sample.

3. The method according to claim 1 wherein the tolerance value is between about ten microns and one thousand microns.

4. The method according to claim 1 further comprising:

identifying a plurality of areas of interest within the sample; and

ranking the plurality of areas of interest in an order.

5. The method according to claim 1 wherein the sample comprises a cytological specimen deposited on a slide.

6. The method according to claim 5 wherein the area of interest within the sample comprises an abnormal cell.

7. The method according to claim 1 wherein the sample is mounted on a stage.

8. The method according to claim 1 further comprising rejecting the sample if the location of the area of interest is not verified.

9. The method according to claim 1 further comprising placing a visible indicator proximate the area of interest identified within the sample.

10. A method for verifying a location of an area of interest within a sample, the method comprising:

locating a datum mark on the sample;

assigning a reference coordinate value to a location of the mark;

identifying an area of interest within the sample;

assigning a coordinate value to the location of the area of interest; and

spatially relocating the mark, thereby determining a spatial offset value of the relocated mark relative to the reference coordinate value;

wherein the location of the area of interest is verified if the spatial offset value is less than a tolerance value.

11. The method according to claim 10 wherein the first locating of the datum mark comprises centering the mark in a field of view of an optical instrument.

12. The method of claim 10 further comprising storing in memory the coordinate value of the area of interest.

13. The method according to claim 10 further comprising:

transferring the sample to a review station;

locating the datum mark; and

setting a coordinate system of the review station based on a location of the mark.

14. A method for verifying a location of an area of interest within a cytological specimen on a slide located in an automated cytological imaging system, the method comprising:

- placing the slide within an optical path of the imaging system;
- centering a datum mark on the slide within a field of view of the imaging system;
- assigning a reference coordinate value to a location of the mark;
- storing in memory the reference coordinate value;
- scanning the specimen to identify an area of interest within the specimen;
- centering the area of interest within the field of view of the imaging system;
- assigning a coordinate value to the area of interest;
- returning to the reference coordinate value location;
- spatially relocating the mark; and
- comparing the reference coordinate value to a coordinate value resulting from spatially relocating the mark, thereby determining a spatial offset value of the mark, wherein the location of the area of interest is verified if the spatial offset value is less than a tolerance value.

20. An imaging system for verifying a location of an area of interest within a sample, the imaging system comprising:

- an optical system; and
- a stage movable relative to the optical system, at least one of the optical system and the stage being operable to position the sample in an optical path of the optical system,

wherein the imaging system is capable of spatially locating a datum mark on the sample and determining a spatial offset of the mark relative to a nominal position thereof.

21. The imaging system according to claim 20 wherein the sample is a cytological specimen deposited on a slide.

23. The method of claim 14 wherein the method is performed while the slide is continuously mounted within the imaging system.

24. A method for verifying a location of an area of interest within a cytological specimen on a slide located in an automated cytological imaging system, the method comprising:

locating a datum mark on the sample;

identifying the area of interest within the sample;

determining the location of the area of interest relative to the mark; and

relocating the datum, wherein the location of the area of interest is verified if a dimensional error in locating the datum relative to relocating the datum is less than a tolerance value.

25. The method of claim 24, wherein the method is performed while the slide is continuously mounted within the imaging system.



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Group Art Unit: 2623

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APPEAL BRIEF TRANSMITTAL

Mail Stop Appeal Brief - Patents

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

Sir,

Transmitted herewith is Appeal Brief (15 pages) in triplicate, for the above-identified application.

The items checked below are appropriate.

- ☒ Appeal Brief Fee:
- ☒ Large Entity Fee of \$500.00; or
- ☐ Small Entity Fee of \$250.00.
- ☐ Applicant(s) claim Small Entity Status under 37 CFR § 1.27.
- ☒ Return Receipt Postcard

CERTIFICATE OF MAILING

I hereby certify that this paper (along with any referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as First Class Mail in an envelope addressed to the Commissioner for Patents, Mail Stop Appeal Brief - Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

4/5/05

Date

Jocelyn L. Lee


Jocelyn L. Lee

- ☒ Please charge Bingham McCutchen's Deposit Account No. **50-2518** in the amount of \$500.00.
- ☒ The Commissioner is authorized to charge Bingham McCutchen's Deposit Account No. **50-2518** for any fees required that are not covered, in whole or in part, and to credit any overpayments to said Deposit Account No. **50-2518**

Respectfully submitted,

BINGHAM McCUTCHEN LLP

Dated: 4/5/05

By: 
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23639
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